



Systematic use of isolated pancreatic anastomosis after pancreatoduodenectomy: Five years of experience with zero mortality

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Abstract

Objective: The aim of this study is to perform a comprehensive evaluation of 5 years of experience with the technique of isolated pancreatic anastomosis reconstruction after pancreatoduodenectomy from the perspective of safety and surgical efficacy using a prospective database.

Methods: The study included all consecutive patients undergoing pancreatoduodenectomy from April 2009 to April 2014 at a single referral center for hepato-pancreato-biliary diseases. The primary endpoint was the safety of the procedures, which was assessed as the occurrence of complications during hospitalization. Ninety-day mortality was also assessed. Postoperative pancreatic fistulas were classified as grade A, B, or C according to the International Study Group of Pancreatic Fistula classification.

Results: The study group included 214 consecutive patients with a median age of 60 years who underwent pancreatoduodenectomy. Portal vein resection was performed on 41 patients. Indications for resection were 165 pancreatic head tumors, 33 ampullary tumors, 7 chronic pancreatitis, 3 distal bile duct tumors, and 6 duodenal tumors. There was no perioperative or 90-day mortality in this series. Complications occurred in 68 patients (32%), and 42 patients presented with pancreatic fistulas (19.6%). Grade A fistulas were present in 38 patients. Three patients presented persistent pancreatic fistula and were treated with percutaneous drainage. One patient developed combined pancreatic and biliary fistulas and was reoperated on for pancreatic abscess drainage.

Conclusions: The technique of isolated pancreatic anastomosis by diverting the pancreatic from biliary secretion may contribute to reducing the severity of pancreatic fistulas and therefore the severity of this complication.

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Keywords: Pancreas; Technique; Reconstruction; Double loop; Isolated

Introduction

Pancreatoduodenectomy (PD) is an established procedure for the treatment of benign and malignant diseases located at the pancreatic head and periampullary region. Although many techniques have been devised to reduce the rate of postoperative complications after PD, postoperative morbidity remains a major concern. The morbidity rate is 40–50% of patients, even in highly specialized centers.^{1–3} The most important postoperative complication is pancreatic fistula.^{3,4} Perioperative complications are even higher in low-volume centers, and mortality is a serious

problem.^{5,6} Most of the complications after PD are related to pancreatic fistulas. Many strategies have been developed to reduce these complications, such as the use of octreotide, duct stents, and many other techniques for reconstruction of the alimentary tract.^{7–15}

In some patients, the outcome of pancreatic fistula is benign, whereas other patients may have an extremely severe or even fatal outcome after developing postoperative pancreatic fistulas. The actual mechanism for this difference in outcomes may be the activation of pancreatic juice by biliary secretion. In order to decrease morbidity and mortality rates after PD, we devised a unique technique using two different jejunal loops for hepatico- and pancreatico-jejunostomy.¹¹ This technique has significantly decreased the severity of complications for our patients. Several modifications of the technique that maintain the

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main principle have subsequently been published and confirmed our initial results.^{12–17}

The aim with this study is to perform a comprehensive evaluation of 5 years of experience with this technique from the perspectives of safety and surgical efficacy using a prospective database. The study is also aimed at providing a technical description of isolated pancreatic anastomosis reconstruction.

Methods

Study design and setting

This observational study analyzed a cohort of patients at an urban referral center for HPB surgery in São Paulo, Brazil. All patients undergoing pancreatic resection at our institution were recorded in a database, which is prospectively maintained by our HPB fellows and clinical study nurses and is presented to a multidisciplinary tumor board. High-quality CT scans and/or MRI preoperative imaging is routinely performed. Coronal and sagittal views are essential for evaluating vascular encasement. If involvement less than 180° of the superior mesenteric artery or short segment hepatic artery involvement at the gastroduodenal artery (GDA) or short segment involvement of the portal vein (<3 cm) is found, the patient is considered borderline Katz type A according to the classification proposed by the MD Anderson group.¹⁸ These patients are referred for neoadjuvant chemotherapy and reevaluation. Portal involvement is considered a contraindication for surgery if the SMV-portal axis is occluded for more than 3 cm or there is not patent SMV or PV above and below the occlusion. These patients as well as those with intravascular tumoral thrombus are considered nonresectable and are referred for radiochemotherapy, although with a surgical reevaluation of the status of the PV-SMV axis.

Consecutive patients undergoing open pancreatoduodenectomy by this team in the 5-year period between April 2009 and April 2014 were retrospectively studied. One of the two authors was the senior surgeon in all procedures. Patients with intraoperative diagnosis of liver metastases or peritoneal implants were excluded from the analysis (Fig. 1).

Surgical technique

The operation starts with a complete exploration of the abdominal cavity to rule out peritoneal and/or liver metastasis. Pancreatic dissection is performed after opening the retrocavity and performing the Kocher maneuver. After division of the gastroepiploic vessels, the duodenum is transected 2 cm below the pylorus with linear stapler. All patients except for 6 cases of duodenal cancer underwent pylorus-preserving pancreatoduodenectomy. In those 6 cases, distal gastrectomy was performed and reconstruction

was done in the same way, but with gastrojejunal anastomosis instead. Cholecystectomy is performed, and the common bile duct is dissected and divided.

The hepatoduodenal ligament is skeletonized, the gastroduodenal artery is divided, and the portal vein is exposed above the pancreas. A tunnel is carefully created behind the neck of the pancreas, and the pancreas is divided. The jejunum is divided with a stapler 20 cm distal to the Treitz ligament. Finally, the uncinate process is carefully dissected from the superior mesenteric vein and the artery, and PD is completed. In cases with known involvement of the portal vein, pancreatic resection begins with superior mesenteric artery dissection, technique that was previously described by our group¹⁹ and subsequently popularized under the name “artery-first technique”.²⁰ Another indication for performing artery-first dissection is the presence of a displaced common or right hepatic artery from the superior mesenteric trunk.

After pancreatic head resection, a double-layered retrocolic end-to-side pancreaticojejunostomy is performed with duct-to-mucosa anastomosis using running monofilament sutures and a second layer between the jejunal seromuscular and pancreatic tissue to reinforce the anastomosis. In smaller ducts, interrupted sutures are used. Pancreatic stents are used in soft glands or in ducts smaller than 3 mm.

Next step is to create a Roux-en-Y limb using a single stapler firing, as previously reported.²¹ A 40-cm jejunal loop is left for the biliary reconstruction (Fig. 2). This biliary loop is brought through another opening in the mesocolon for use in biliary reconstruction. Hepaticojejunostomy is usually performed with end-to-side running 5-0 PDS suture. Finally, an end-to-side duodenojejunal anastomosis is performed 30 cm downstream from the Roux-en-Y using the standard double-layer technique in an antecolic fashion (Fig. 2). Abdominal cavity drainage is also done separately. Two drains are used and exteriorized on either side of abdominal cavity.

Variables

The primary endpoint of this study is the safety of this procedure, which was assessed as the occurrence of complications during hospitalization (Dindo-Clavien classification) as well as a 90-day mortality. Postoperative pancreatic fistulas were classified as grade A, B, or C according to the International Study Group of Pancreatic Fistula classification.²² The recently published comprehensive complication index (CCI) to explore a different system for severity of complications.²³ Secondary outcomes were surgical efficacy endpoints such as conversion rates, operative times, blood loss, need for transfusions, proportion of positive margins, and hospital length of stay.

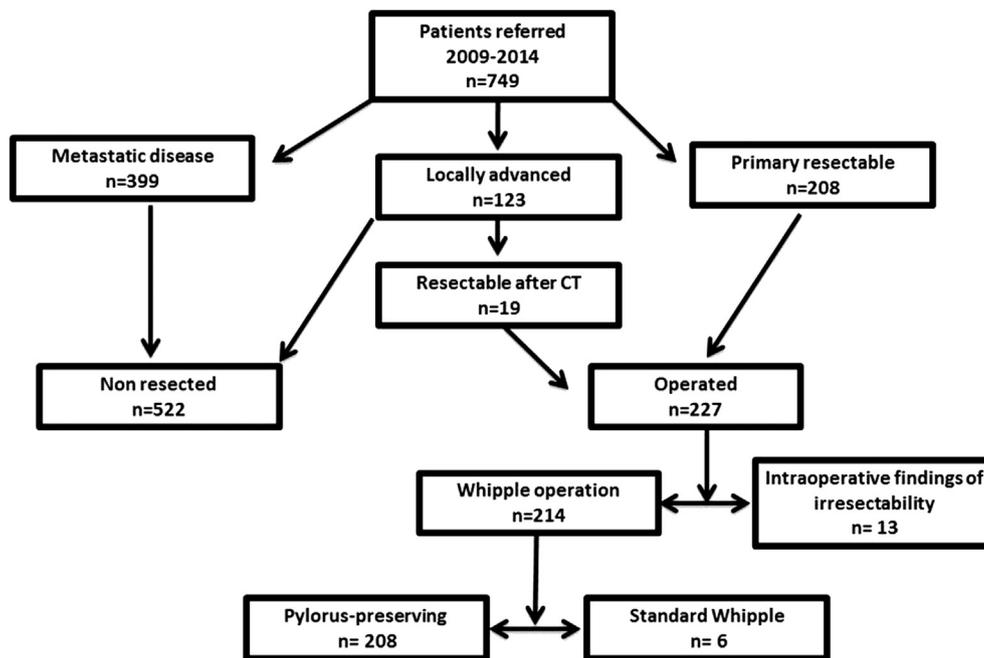


Figure 1. Flow diagram showing all referred patients for pancreatoduodenectomy in our institution between 2009 and 2014 and stratified by resectability and type of operation. CT – chemotherapy.

Results

As in any retrospective cohort study, it identified an era and selection bias that may have contributed to a better outcome.

Participants

The study group included 214 patients with a median age of 60 years (range: 20–83 years) who underwent pancreatoduodenectomy. Patient demographics and preoperative parameters are depicted in Table 1. Indications for resection were 165 pancreatic head tumors, 33 ampullary tumors, 7 chronic pancreatitis, 3 distal bile duct tumors, and 6 duodenal tumors (Table 2). TNM stage was depicted in Table 3. Among all patients referred for surgery, 19 were found resectable after neoadjuvant chemotherapy and 13 were not resected after intraoperative findings of irresectability (Fig. 1). Four patients presented peritoneal implants

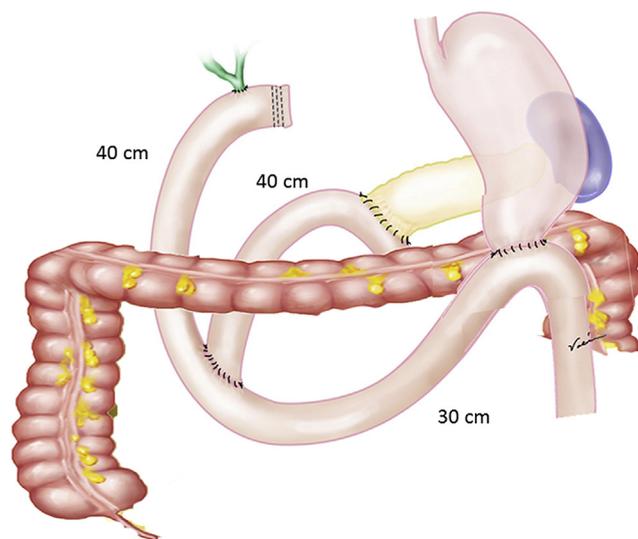


Figure 2. Schematic drawing of isolated pancreatic anastomosis technique for reconstruction of the alimentary tract after pancreatoduodenectomy. Roux-en-Y limb is created. One jejunal loop (40 cm) is brought through the mesenteric window for pancreatic anastomosis, and another loop (40 cm) in another window is used for biliary reconstruction. Distal jejunum is used for duodenojejunal anastomosis in an antecolic fashion performed 30 cm downstream from the Roux-en-Y.

Table 1
Patient demographics and comorbidities.

Demographics and preoperative parameters	
Age, median (range), y	60 (20–83)
Gender, Male:Female, n	118:96
Jaundice, n (%)	143 (67)
Weight loss, n (%)	81 (37.8)
Albumin <3.5 g/dL, n (%)	41 (19.1)
Weight loss > 10%, n (%)	32 (14.9)
BMI, mean \pm SD, kg/m ²	26.2 \pm 2.2
Malnutrition ^a , n (%)	14 (6.5)
Hypertension, n (%)	65 (30.4)
Diabetes, n (%)	48 (22.4)
Smoking, n (%)	92 (43)
Alcohol abuse, n (%)	30 (14)
Prior abdominal surgery, n (%)	43 (20)
Preoperative biliary drainage, n (%)	18 (8.4)

^a Weight loss >10% with albumin <3 or BMI < 20.

Table 2
Pathology and TNM stage.

	n	%
Pathology		
Pancreatic adenocarcinoma	165	77.1
Periampullary adenocarcinoma	33	15.4
Chronic pancreatitis	7	3.2
Duodenal adenocarcinoma	6	2.8
Distal bile duct cancer	3	1.4
TNM stage^a		
Stage 0	1	0.5
Stage IA	5	2.4
Stage IB	21	10.1
Stage IIA	70	33.8
Stage IIB	97	46.9
Stage III	13	6.3

7 patients with chronic pancreatitis were excluded.

^a 7th Edition American Joint Committee on Cancer (AJCC) TNM staging.

and in nine patients liver metastasis were found during abdominal inspection.

Pylorus preservation was possible in 208 patients (97%). In six patients with duodenal cancer, distal gastrectomy was necessary, and standard pancreatoduodenectomy was performed. Portal vein resection was performed in 41 patients (19%), which consisted of lateral venorrhaphy in 25 patients and end-to-end portal reconstruction in the remaining patients (Table 3).

Outcomes

Operative variables and outcomes are summarized in Table 3. There was no perioperative or 90-day mortality

Table 3
Operative variables and complications.

Variable	n
Operative time, mean \pm SD, min	243 \pm 120
Estimated blood loss, mean \pm SD, mL	384 \pm 215
Pylorus-preserving pancreatoduodenectomy, n (%)	208 (97)
Standard pancreatoduodenectomy, n (%)	6 (3)
Portal vein resection, n (%)	41 (19)
Blood transfusion during hospitalization, n (%)	52 (24.3)
Use of pancreatic stent, n (%)	61 (28.5)
ICU stay, mean \pm SD, d	2.2 \pm 1.2
Hospital stay, mean \pm SD, d	9.7 \pm 4.1
Overall Complications, n (%)	68 (32)
Complications \geq IIIA (Clavien-Dindo), n (%)	10 (4.7)
CCI, median (range)	23.5 (0–42.4)
Pancreatic fistula, n (%)	42 (19.6)
Grade A	38
Grade B	3
Grade C	1
Wound infections, n (%)	8 (3.8)
Delayed gastric emptying, n (%)	6 (2.8)
Cardio-pulmonary complications, n (%)	6 (2.8)
Bile leak, n (%)	2 (1)
Post-pancreatectomy bleeding, n (%)	2 (1)
Reoperation, n (%)	2 (1)
Mortality	0

SD = standard deviation, CCI = comprehensive complications index.

in this series. Complications occurred in 68 patients (32%), while 42 patients presented with pancreatic fistula. Grade A fistulas were present in 38 patients (90%). Three patients presented persistent pancreatic fistula (7%) and were treated with percutaneous drainage (grade B). One patient developed a combined pancreatic and biliary fistula and was reoperated on for pancreatic abscess drainage (grade C – 3%). Two other patients were reoperated due to internal hernia with obstruction and bowel ischemia. One patient developed gastroduodenal artery pseudoaneurysm, which was treated by endovascular prosthesis. Six patients presented delayed gastric emptying. All of these patients recovered uneventfully. One patient developed biliary stenosis that required reoperation 6 months after pancreatic resection after failure of percutaneous dilatation.

Discussion

Despite recent advances in surgical procedures and post-operative management techniques, pancreatoduodenectomy still carries a considerable postoperative morbidity and mortality. The mortality rate is likely higher in low volume hospitals.^{5,25} Highly specialized medicine in high volume centers seems to be the key to provide a better outcome for these patients, but it has been implemented only in a few highly developed countries.^{26,27} The present data are from highly experienced pancreatic surgeons in a high-volume institution (with a mean of 45 Whipple procedures per year) from a developing country. Similar to other experiences the mortality rate in our department was around 40% in the 1970s,¹¹ leading some authors to suggest that its use be abandoned.^{28,29} At this time the simple change in the technique with the systematic use of an isolated pancreatic anastomosis resulted in a sharp decrease in the postoperative mortality to 5%.³⁰ Later on, Funovics et al.³¹ in an analysis of three different techniques for reconstruction after pancreatoduodenectomy concluded that the use of separate intestinal loops offers the best technical solution to the morbidity of this operation.

Since then, several other techniques and advances in the surgical field resulted in a rapid decline in the mortality rate worldwide. However, pancreatic fistula is still the most common factor responsible for the high morbidity and mortality after pancreatoduodenectomy.³² To reduce the incidence and complications of this anastomosis, several techniques have been used, such as pancreaticogastrostomy, duct-to-mucosa anastomosis, binding pancreatojejunostomy, perioperative administration of somatostatin analogs, and the use of adhesive sealants, among others. However, no advantages have been shown of one technique over another.¹

Variations of pancreatojejunostomy have been evaluated, and lower pancreatic fistulas rate were seen in the invagination technique, especially in the soft pancreas.³³ In other studies, superiority was demonstrated for duct-to-mucosa anastomosis.³⁴ Other variations of pancreatic reconstruction have

also been investigated.³⁵ Compared with pancreatojejunostomy, pancreatogastrostomy does not show any significant differences in the overall postoperative complication rate or incidence of pancreatic fistula.^{9,10} Since a reliable technique for pancreatojejunostomy has not been devised, additional managements have been used to decrease the incidence or severity of pancreatic fistulas. In some studies, external drainage of the pancreatic duct with a stent reduced the rate of pancreatic fistula after pancreatojejunostomy, mainly in patients with soft glands.^{20,36}

Most of the reports related to pancreatic fistula were performed without a standardized definition of pancreatic fistula and its newly introduced grading system and focused decreasing the incidence and not to the severity of the complication.¹⁷ Pancreatic juice is secreted in an inactivated state and is activated in the bowel lumen by mainly biliary secretion. In the event of a pancreatic fistula in a patient with an isolated pancreatic anastomosis, the leak will consist of inactive pancreatic enzyme precursors that are not associated with serious complications.^{37,38} An important and sometimes neglected is the adequate length (40 cm) of the jejunal loop. We found however that another essential point is placing two separated drains to isolate the drainage fluids from the rest of the operative field, one adjacent to the pancreatic stump and another near the biliary anastomosis. Biliary pancreatic secretion activation is in our opinion the main factor responsible for the severity of pancreatic fistula. We induced this from the simple observation that postoperative mortality is extremely high in patients with combined biliary and pancreatic fistulas after pancreatoduodenectomy.³⁹ We presume that the use of a single jejunal loop for biliary and pancreatic anastomosis leads to the activation of proteolytic enzymes and consequent tissue damage. Separation of the biliary and pancreatic conduits may decrease the severity of pancreatic fistulas,^{11,13,14} therefore reducing the morbidity and mortality of pancreatoduodenectomy. This was the rationale behind the double jejunal loop technique first description in 1976. The morbidity remained 60% with 50% of pancreatic complications but the mortality decreased from 40 to 5% at the time.³⁰ This assumption was then demonstrated by Ke et al.¹⁷ Their prospective randomized study showed that isolated pancreatic anastomosis was not associated with a lower incidence of pancreatic fistula in comparison with conventional reconstruction but it contributed to decreasing fistula severity, duration of stay, and hospital expense.¹⁷ We are supporting the findings of this randomized study with our clinical audit of a consecutive series of 214 patients to show that the majority of patients in the present series who developed pancreatic fistula had a grade A pancreatic fistula.

Additional benefits of isolated pancreatic anastomosis are the prevention of chronic biliary duct damage from pancreatic juice reflux, which may cause epithelial erosion dysplasia and cholangiocarcinoma.⁴⁰ This may be important for young patients operated on for benign or low-grade malignancy with expected long-term survival. Although there is no evidence of this hypothetical risk,

there are single case reports of “de novo” cholangiocarcinoma after pancreatoduodenectomy for distal bile duct cancer.^{41,42} Another advantage of this type of alimentary reconstruction is related to the eventual need for reoperation for biliary or pancreatic anastomosis complications, such as stenosis.⁴¹ Reoperation in this setting may be easier and safer when separate loops have been used.

One point of criticism is that the use of this technique is time-consuming. This may be overcome with the use of the single-firing stapler technique.²¹ We are aware that the isolated pancreatic anastomosis technique may be undervalued by some high volume centers.⁴⁰ We suggest however this technique may further reduce complications even in these high-volume centers. Certainly our technique appears useful in situations where high morbidity and mortality are expected after pancreatoduodenectomy. The typical situation to utilize this technique is when the pancreas is soft and the pancreatic duct is small. Another typical situation arises when Whipple procedures are performed in low-volume centers or by inexperienced surgeons.^{43–45} In both scenarios this technique that may decrease morbidity and mortality despite the fact that we recommend referral to high volume centers.

Due to the success with this technique we utilize this type of reconstruction also been used in our laparoscopic pancreaticoduodenectomies with similarly satisfying results.⁴⁴ Other surgical center have had no mortality or no pancreatic complications in their consecutive series of pancreatoduodenectomy.^{45–50} According to Samra et al.,⁴⁹ a multidisciplinary team was the key to avoiding mortality, even after 19% of severe postoperative complications. Even in middle-volume centers, it is possible to have zero-mortality after PD.⁵⁰ In the Johns-Hopkins experience with 650 patients, operative mortality was 1.4%, but they also reported a consecutive series of 190 patients without mortality was seen during the period of study. Pancreatic fistula occurred in 14% of patients.⁴⁸ One study by Sutton et al. using isolated pancreatojejunostomy achieved a pancreatic leak rate of zero.⁴⁵ Of course good outcomes after the Whipple procedure are indeed multifactorial and are certainly never cause by a single surgical technique. The multidisciplinary approach, high volume and standardization of the technique contributed also to improve outcome in our series over time. Our objective is not to keep zero mortality since may well not be realistic for a long period as already published.⁴⁸

The current study has several limitations, in particular, the retrospective nature of the study and a potential era bias. Additionally all patients were treated in a high-volume center after evaluation by a multidisciplinary team, which may well introduce a selection bias. Despite this, we found the clinical audit helpful to evaluate out subjective impression that outcomes had improved after we introduced the standard use of the isolated pancreatic anastomotic technique.

In conclusion, our retrospective clinical audit shows that while our cohort is comparable to series of pancreaticoduodenectomies in the published literature, our

complication and mortality rates are comparatively low and the severity of postoperative pancreatic fistulas are fairly mild. The isolated pancreatic anastomosis technique by diverting the pancreatic from biliary secretion may contribute to reducing the severity of pancreatic fistula and the dangerous sequelae of this complication.

Conflict of interest statement

The authors declare no conflicts of interest.

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